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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: POLYPEPTIDES WITH A SIGNAL SEQUENCE COMPRISING AN FIVSI MOTIF AND OLYNUCLEOTIDES ENCODING THEREFOR

pre	Pro	pre-albumin		pro region
HSA	HSA	Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Ser Ser Ala Tyr Ser Arg Gly Val Phe Arg Arg		
HSA	MFa-1	Met Lys Trp Val Thr Phe Ile Ser Leu Leu Phe Ser Ser Ala Tyr Ser Arg Ser Leu Asp Lys Arg		
		-24 -23 -22 -21 -20 -19 -18 -17 -16 -15 -14 -13 -12 -11 -10 -9 -8 -7 -6 -5 -4 -3 -2 -1		

preferred mutations
of the invention: Phe Ile Val Ile

WO 2004/009819 A3

(57) Abstract: The present invention provides a polypeptide comprising (i) a leader sequence, the leader sequence comprising a (a) secretion pre sequence, and (b) the following motif: -X₁-X₂-X₃-X₄-X₅, where X₁ is phenylalanine, tryptophan, or tyrosine, X₂ is isoleucine, leucine, valine, alanine or methionine, X₃ is leucine, valine, alanine or methionine, X₄ is serine or threonine and X₅ is isoleucine, valine, alanine or methionine; and (ii) a desired protein heterologous to the leader sequence. A polypeptide of the invention may additionally comprise, as part of the leader sequence, a secretion pro sequence. The invention also provides a polynucleotide comprising a sequence that encodes a polypeptide of the invention and a cell, preferably a yeast cell, comprising said polynucleotide.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/62 C12N15/67 C12N15/81 C07K14/765 C07K14/79

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, SEQUENCE SEARCH, PAJ, WPI Data, BIOSIS, EMBASE, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 53051 A (GENSET SA ; DUCLERT AYMERIC (FR); DUMAS MILNE EDWARDS JEAN BAPTISTE (F) 21 October 1999 (1999-10-21) SEQ ID NO: 1540; SECRETORY PROTEIN; HUMAN CLONE 752 PRECURSOR N-TERMINAL FRAGMENT --- WO 90 01063 A (DELTA BIOTECHNOLOGY LTD) 8 February 1990 (1990-02-08) cited in the application the whole document ---	1-10, 12-29, 36, 38-50
X	---	1-6, 8-10, 12-16, 20-27, 29, 36, 38-52

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

11 December 2003

Date of mailing of the International search report

15/01/2004

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 02 083876 A (GIETZEN DARRYL; INCYTE GENOMICS INC ; TRAN ALANNA-PHUNG B (US); DAF) 24 October 2002 (2002-10-24) SEQ ID NO: 1025, SEQ ID NO: 447 page 74; claims page 211 page 444 ---	1-10, 12-29, 36, 38-52
P,X,L	DATABASE REGISTRY 'Online! retrieved from REGISTRY Database accession no. 473511-23-8 XP002264012 L: INFORMATION ON SEQUENCE ID: 1025 FROM WO02083876 abstract ---	1-10, 12-29, 36, 38-50
E	WO 03 066824 A (HAUSER HANS-PETER ;WEIMER THOMAS (DE); AVENTIS BEHRING GMBH (DE);) 14 August 2003 (2003-08-14) SEQ ID NO: 108 page 68; claims page 81 page 85 ---	1-29, 36, 38-50
E	WO 03 066078 A (HAUSER HANS-PETER ;WEIMER THOMAS (DE); AVENTIS BEHRING GMBH (DE);) 14 August 2003 (2003-08-14) SEQ ID NO: 37, 41 claims; figures 1,2,5,6 ---	1-29, 36, 38-50
E	WO 03 066085 A (HAUSER HANS-PETER ;CELIK ILHAN (DE); KISKER OLIVER (DE); MERTINS P) 14 August 2003 (2003-08-14) SEQ ID NO: 31, SEQ ID NO: 35, SEQ ID NO: 39 figures 1,2,5,6,9,10 ---	1-29, 36, 38-50
A	PARKHILL J ET AL: "Complete genome sequence of a multiple drug resistant salmonella enterica serovar typhi CT18" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 413, 25 October 2001 (2001-10-25), pages 848-852, XP002965014 ISSN: 0028-0836 -& DATABASE EMBL 'Online! retrieved from EBI Database accession no. CAD09246 XP002264013 abstract ---	1-10, 12-16, 20
A	----- -/-	1-10, 12-16, 20

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SLEEP D ET AL: "THE SECRETION OF HUMAN SERUM ALBUMIN FROM THE YEAST SACCHAROMYCES-CEREVISIAE USING FIVE DIFFERENT LEADER SEQUENCES" BIO-TECHNOLOGY (NEW YORK), vol. 8, no. 1, 1990, pages 42-46, XP002264011 ISSN: 0733-222X the whole document -----	1-52
A	OKABAYSHI K ET AL: "SECRETORY EXPRESSION OF THE HUMAN SERUM ALBUMIN GENE IN THE YEAST, SACCHAROMYCES CEREVISIAE" JOURNAL OF BIOCHEMISTRY, JAPANESE BIOCHEMISTRY SOCIETY, TOKYO, JP, vol. 110, no. 1, 1991, pages 103-110, XP000610608 ISSN: 0021-924X the whole document -----	1-52
A	SLEEP D ET AL: "Saccharomyces cerevisiae strains that overexpress heterologous proteins" BIO/TECHNOLOGY, NATURE PUBLISHING CO. NEW YORK, US, vol. 9, 1 February 1991 (1991-02-01), pages 183-187, XP002085129 ISSN: 0733-222X the whole document -----	1-52

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Box 1 Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

 2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

 3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple Inventions in this International application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
 2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
 3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: _____
 4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the Invention first mentioned in the claims; it is covered by claims Nos.: _____

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-6,8-10,12-16,20-27,29 and 38-52 relate to an extremely large number of possible compounds, namely the polypeptide disclosed in claim 1. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to a peptide comprising the motif -Phe-Ile-Val-ser-Ile- (FIVSI).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No	PCT/GB 03/03273
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